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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/674,787      | 10/01/2003  | Hideobu Yaku         | 061352-0045         | 3667             |

20277 7590 10/16/2006

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| EXAMINER |
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CHUNDURU, SURYAPRABHA

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| ART UNIT | PAPER NUMBER |
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1637

DATE MAILED: 10/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/674,787

Applicant(s)

YAKU ET AL.

Examiner

Suryaprabha Chunduru

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 10 August 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-12, 19-27 and 31-33 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-12, 19-27 and 31-33 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 December 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 8/4/06.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_.

**DETAILED ACTION**

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 10, 2006 has been entered.

***Status of the Application***

2. The action is in response to the RCE filed on August 10, 2006. Currently claims 1-12, 19-27, 31-33 are pending. Claims 13-18 and 28-30 are cancelled. New claims 31-33 are added. All arguments and amendment have been fully considered and thoroughly reviewed and deemed persuasive for the reasons that follow.

***New Grounds of Rejections***

***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-12, and 19-27, 31-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Orlefors et al. (WO 00/40750) in view of Maeshima (Biochemica et Biophysica Acta, Vol. 1465, No. 1-2, pp. 37-51, May 2000).

Orlefors et al. teach a method of claims 1-2, 8, and 19, of detecting an extension reaction and identifying a base at a target nucleic acid sequence (discriminating a base type) or detecting a base sequence of a target nucleic acid, wherein Orlefors et al. disclose that said method comprises

(a) preparing a sample solution containing a nucleic acid, a primer having a base sequence that is complementary to said target nucleic acid and at least a dATP or ddATP (page 17, line 3-9, page 4, line 15-25, page 17, line 34, page 18, line 1-12);

(b) allowing said sample solution to stand under conditions that cause said extension reaction and producing pyrophosphate (PPi) when said extension is caused (see page 17, line 3-10, page 4, line 24-25, page 18, line 1-12);

(c) measuring the release of PPi and detecting the extension of DNA sequence and identifying the base added by measuring the release of PPi and detecting the sequence of said target DNA (see page 17, line 11-12, page 4, line 26-32, page 17, line 34, page 18, line 13-17).

With regard to claims 1-2, 5, and 19 Orlefors et al. also teach that said method detects extension products and identifies single base polymorphisms (base discrimination) and base sequence of the target nucleic acid (see page 5, line 20-26, page 17, line 11-12, page 17 line 34, page 18, line 1-17).

With regard to claim 7, Orlefors et al. teach use of a different nucleotides to discriminate a base type (see page 19, line 10-11).

With regard to claims 11, and 26, Orlefors et al. teach that the PPi release is measured as a primer extension product produced, which is detected electrically (see page 9, line 6-33, page 10, line 1-31, page 16, line 1-10);

With regard to claim 12, and 27, Orlefors et al. teach that said extension reaction is performed using polymerase chain reaction (PCR) (see page 10, line 4-12, page 17, line 1-34, page 18, line 1-17)

However, Orlefors et al. did not specifically teach contacting sample solution with a permeable membrane having  $H^+$  pyrophosphatase which hydrolyses pyrophosphate released during extension reaction and measuring the  $H^+$  concentration either in solution on the front face of the membrane or in the solution at the back face of the membrane.

Maeshima teaches that PPI is the substrate for  $H^+$  pyrophosphatase ( $H^+$  -PPase), which is produced as a by-product of several metabolic processes such as polymeraization of DNA and RNA (see page 38, col. 1, line 21-27) and measuring the activity of said enzyme based on PPi hydrolysis (see page 39, col.1, section 2-2) measuring ( $H^+$  -PPase) electrochemically in a pH gradient across vacuolar membranes (see page 40, col. 2, paragraph 1). Maeshima also teaches that the active synthesis in growing tissue results in large amount of PPi production as a by-product, which is scavenged by vacuolar  $H^+$  -PPase and is used as a source of energy for active transport of protons into the expanding vacuoles (see page 45, col. 1, paragraph 1, Fig. 4).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of detecting extension product or base sequence

based on PPi release as disclosed by Orlefors et al. with the step of including membrane associated H<sup>+</sup> pyrophosphatase to measure PPi release as disclosed by Maeshima for the purpose of developing a sensitive method for stably detecting base extension reaction or polymerization reaction of a target nucleic acid. An ordinary person skill in the art would have been motivated to combine the method taught by the Orlefors et al. with the inclusion of vacuolar membrane associated H<sup>+</sup> pyrophosphatase to measure the release of PPi to achieve expected advantage of developing a sensitive method for detecting base sequence of a target nucleic acid. The ordinary artisan would have a reasonable expectation of success that the inclusion of said vacuolar membrane associated H<sup>+</sup> pyrophosphatase would result in a sensitive measurement of PPi released during extension reaction by measuring H<sup>+</sup> concentration on at least either one side of the membrane because Maeshima explicitly taught that the by-product produced by polymerization of DNA or RNA is scavenged by vacuolar H<sup>+</sup> -PPase, and uses it as a source of energy for transporting protons into the vacuoles (see page 38, col. 1, line 21-27, page 45, col. 1, paragraph 1, Fig. 4) and such modification of the method would be obvious over the cited prior art in the absence of secondary considerations.

#### ***Double Patenting***

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-12, 19-27, 31-33 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3-9, 14-19 of copending Application No. 10/727,664 (Pub No. US 2004/0197803). Although the conflicting claims are not identical, they are not patentably distinct from each other because an obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims 1-12, 19-27, and 31-33 are generic to all that is recited in claim 1 in combination with claims 3-9, 14-15 of the co-pending application. That is, the claim 1 in combination with claims 3-9, and 14-15 of the co-pending application fall entirely within the scope of claims 1-12, 19-27, and 31-33 or in other words, claims 1-12, 19-27, and 31-33 are anticipated by the claim 1 in combination with claims 3-9, 14-19 of the co-pending application. Specifically the method of steps (a) through (e) disclosing a method of detecting extension or base type or base sequence in a target nucleic acid comprising a primer extension reaction and measuring the release of pyrophosphate and measuring  $H^+$  concentration using a permeable membrane having  $H^+$  pyrophosphatase and detecting extension product based on the measurement of  $H^+$  concentration of the claim 1 in combination with 2-9, 14-19 the claim 23 of

the co-pending application are within the scope of the instant claims 1-12, 19-27, and 31-33. Further the instant claims 9-11, 24-26, and 31-33 are generic to all that is recited in the claims 16-19 of the co-pending application, in other words, the instant claims 9-11, and 24-26 are anticipated by claims 16-19, that is claims 16-19 of the co-pending application fall entirely within the scope of the instant claims 9-11, 24-26, and 31-33. Thus the instant claims encompass the claims in the co-pending application and are related as genus and species, and are coextensive in scope.

The courts have stated that a genus is obvious in view of the teachings of a species. see Slayter, 276 F.2d 408, 411, 125 USPQ 345, 347 (CCPA 1960); and In re Gosteli, 872 F.2d 1008, 10 USPQ2d 1614 (Fed.Cir. 1989). Therefore the instantly claimed method is obvious over the claims in the co-pending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Response to arguments:***

5. With regard to the rejection made in the previous office action under 35 USC 103(a) as being unpatentable over Clark et al. in view of Zhen et al., Applicants' arguments are fully considered and the rejection is moot in view of the arguments and new grounds of rejections. To address the arguments made toward the measuring PPI released as a result of primer extension, Examiner presents new rejections as set forth above.

6. Applicants' response to the previous office action did not address rejection maintained under provisional double patenting, Examiner reiterates that the submission of a terminal disclaimer is



improper for referring to an incorrect serial No. of the co-pending reference application number.

The rejection is maintained until a proper terminal disclaimer is submitted.

***Conclusion***

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M , Mon - Friday,.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Suryaprabha Chunduru  
Primary Examiner  
Art Unit 1637

*Suryaprabha Chunduru*  
10/11/06  
SURYAPRABHA CHUNDURU  
PATENT EXAMINER